



NOTES

MOVEMENT DISORDERS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Disorders causing abnormal movement
 - Increased voluntary/involuntary movement (hyperkinetic disorders); reduced movement (hypokinetic disorders)

TYPES

Acute fulminant episodes

- Reaction to trigger, medication (neuroleptic malignant syndrome)

Benign chronic conditions

- Restless legs syndrome (RLS), essential tremor

Progressive chronic syndromes

- Parkinson's disease (PD), Friedreich's ataxia

CAUSES

- Often idiopathic; genetic mutations, medication

SIGNS & SYMPTOMS

- Mild, unpleasant sensations, intention/action tremors; rigidity, catatonia

- Motor abnormality
 - Hypokinesia:** ↓ amplitude
 - Bradykinesia:** ↓ speed
 - Dyskinesia:** unwanted, characterized motor movement
 - Tremor:** rhythmic motor movement; resting, action, postural
 - Rigidity:** abnormal, uncoordinated muscle tone across joint

DIAGNOSIS

OTHER DIAGNOSTICS

- Neurologic examination
 - Observation of spontaneous movement, strength testing, tone evaluation, reflex exam

TREATMENT

MEDICATIONS

- Beta blockers, anti-epileptics, benzodiazepines; dopamine replacement, agonists

OTHER INTERVENTIONS

- Avoid caffeine, nicotine, etc.
- Educational, supportive therapy

VISIT...

LANZAROTE
Caliente.COM

ESSENTIAL TREMOR

osms.it/essential-tremor

PATHOLOGY & CAUSES

- Most common movement disorder; involuntary, rhythmic shaking
- Usually affects hands, fingers; sometimes head, vocal cords
- Action tremor (occurs during muscle effort)
 - Postural/intention tremor

CAUSES

- Unknown; may be familial with autosomal dominant inheritance pattern

RISK FACTORS

- Meat consumption
 - Exposure to heterocyclic amines (e.g. harmane, harmaline)
- Associated with dystonia (cervical, spasmodic, cranial dystonia, writer's cramp), parkinsonism

SIGNS & SYMPTOMS

- Rhythmic, symmetrical tremor
 - Hands, head, vocal cords, neck, face, leg, tongue, trunk
- High frequency tremor (4–12Hz) exacerbated by muscle contraction
- Inability to perform precise tasks
- Intention tremor
 - Intensifies upon touching nose with finger
- Postural tremor
 - During outstretched arms
- Walking difficulties
- ↓ tremor with alcohol intake

DIAGNOSIS

OTHER DIAGNOSTICS

- Postural/action tremor of hands/head; duration ≥ three year
- Alleviation with alcohol intake

Physical examination

- Fine postural, action tremor in hands, head/voice
- *Asymmetric/symmetric*: cogwheel rigidity, resting tremor, dystonia (esp. head)

TREATMENT

MEDICATIONS

- If disabling, symptomatic treatment
 - Beta blockers
 - Anti-epileptics
 - Benzodiazepines
 - Botulinum toxin (head tremors not responsive to medication)

OTHER INTERVENTIONS

- Avoid caffeine, nicotine, etc.
- Get enough sleep

ESSENTIAL TREMOR VS. PARKINSON'S TREMOR

	ESSENTIAL TREMOR	PARKINSON'S TREMOR
LATERALLY	Symmetrical	Asymmetrical
KINETICS	Movement/posture	Resting
SPEED	High frequency	Slow frequency
INVOLVEMENT	Arms, legs, voice, neck, face, tongue	Hands, legs, chin

FRIEDREICH'S ATAXIA

osms.it/friedreichs-ataxia

PATHOLOGY & CAUSES

- Genetic disorder; causes progressive central nervous system (CNS) damage, movement problems
- Predominantly affects CNS; also affects heart, pancreas
- ↓ frataxin → ↓ mitochondrial oxidative phosphorylation → cell damage, death
- ↓ frataxin → ↑ free iron → ↑ oxidative stress → cell damage, death
- Neuronal cell death affects posterior columns of spinal cord, distal corticospinal tracts, spinocerebellar tracts, brain stem, cerebellum
- Gene silencing → no frataxin synthesized → iron accumulates in cell, reacts with oxygen → unstable oxygen radicals → cell death

CAUSES

- Trinucleotide repeat GAA expansion (chromosome 9q13) → ↓ production of mitochondrial inner membrane protein, frataxin
 - Autosomal recessive inheritance pattern
 - ↑ repeats → ↑ severity, ↓ age of onset

- 600–1200 trinucleotide repeats → Friedreich's ataxia

COMPLICATIONS

Progressive loss of cells

- In CNS, heart, pancreas
- Limb, gait ataxia → wheelchair bound → bedridden
- Dysphagia, dysarthria → aspiration → gastric bacteria insult to respiratory parenchyma
- Hypertrophic cardiomyopathy (secondary to myocardial cell death)
 - Fibrosis → arrhythmia, hypertrophic cardiomyopathy → heart failure
 - Most common cause of death in affected individuals (age 40–50)
- Diabetes mellitus
 - Loss of beta cells of pancreas
- 25% of affected individuals
- Musculoskeletal abnormalities
 - Muscle denervation → abnormal forces about joints → abnormalities
- Kyphoscoliosis
 - Severe → ↓ total lung capacity → restrictive lung disease

- Pes cavus
 - Similar restrictive lung disease in severe cases
- Hammer toes

SIGNS & SYMPTOMS

- Ataxia
 - Falling/staggering while walking, wide-based gait
 - Gait ataxia most common (age 0–10); most individuals progress to wheelchair dependence within 11–25 years
- Loss of vibratory sense, proprioception
- Muscle weakness, chest pain, dyspnea, heart palpitations, absence of tendon reflexes in legs, involuntary eye movements, action tremor, hand clumsiness, dysarthria, fatigue

DIAGNOSIS

LAB RESULTS

Genetic testing

- Confirms diagnosis
- GAA repeats; examine first intron in frataxin gene

OTHER DIAGNOSTICS

- Symptom progression, family history
- Neurological exam
 - Ataxia (gait, hand); ↓ vibratory sensation, proprioception; ↓ deep tendon reflexes, nystagmus

Electromyogram

- Absent/reduced sensory nerve action potentials
- Normal/only slightly decreased motor nerve conduction velocities
- Abnormal auditory, visual, somatosensory-evoked responses

TREATMENT

OTHER INTERVENTIONS

- Occupational, physical therapy
 - Balance, ataxic progression
- Cardiology
 - Annual electrocardiogram, echocardiogram
- Severe scoliosis
 - Orthopedic referral
- Annual diabetes screening
- Genetic, psychological counseling services

NEUROLEPTIC MALIGNANT SYNDROME

osms.it/neuroleptic-malignant-syndrome

PATHOLOGY & CAUSES

- Life-threatening idiosyncratic reaction to antipsychotic drugs; muscle rigidity, fever, altered mental status, autonomic dysfunction
- Dopamine blockade theory
 - Central dopamine blockade → hypothalamus → hyperthermia, dysautonomia
 - Nigrostriatal dopamine blockade → tremor, rigidity
- Peripheral muscle theory
 - Direct toxic effect of neuroleptics → mitochondria of skeletal muscle → rigidity, fever
- Sympathetic nervous system theory
 - ↓ dopamine inhibitors → ↑ sympathetic output
 - ↑ sudomotor, vasomotor activity → fever

CAUSES

Reaction to medications

- First-generation neuroleptic (most common)
 - Haloperidol, fluphenazine, chlorpromazine
- Second-generation neuroleptic medication
 - Clozapine, risperidone, olanzapine
- Antiemetic
 - Metoclopramide, promethazine, droperidol
- Withdrawal of L-Dopa/dopamine agonist therapy (Parkinson disease)

RISK FACTORS

- Increase in dose/change of neuroleptic medication
- Abrupt cessation/reduction of dopaminergic medication

- Lithium/alcohol/psychoactive substance use
- Previous episode of neuroleptic malignant syndrome
- Acute injury (e.g. trauma, surgery, infection)
- Psychiatric conditions (e.g. acute catatonia, severe agitation)
- Lewy body dementia

COMPLICATIONS

- Rhabdomyolysis, renal failure
- Seizures
 - Due to hyperthermia, metabolic imbalances
- Encephalopathy, stupor, coma
- Cardiac arrhythmias (e.g. torsades de pointes, cardiac arrest)
- Disseminated intravascular coagulation

SIGNS & SYMPTOMS

Altered mental status

- Agitated delirium with confusion (initial symptom); coma

Muscular abnormalities

- Generalized muscular rigidity ("lead-pipe rigidity")
 - Associated dysphonia, dysarthria
- Catatonic signs
- Extrapyrimal symptoms
 - Tremor, chorea, akinesia
- Less common
 - Dystonic movements (e.g. opisthotonos, trismus, blepharospasm), mutism, dysarthria, dysphagia

Hyperthermia

- Temperatures > 38–40°C/100.4–104°F

Autonomic dysfunction

- Tachycardia, labile/elevated blood pressure, tachypnea, sialorrhea, profuse diaphoresis (sweating), flushing, incontinence

DIAGNOSIS**LAB RESULTS**

- Severe ↑ creatine kinase (CK)
 - Correlates with rigidity severity → 1–100k international units/L
- Mild ↑ lactate dehydrogenase, alkaline phosphatase, liver transaminases
- Electrolyte imbalances
 - ↓ Ca^{2+} , ↓ Mg^{2+} , ↓ Na^+ /↑ Na^+ , ↑ K^+ , metabolic acidosis
- ↑ white blood cell count (leukocytosis) 10–40k
- Myoglobinuria
- ↓ serum iron concentration

OTHER DIAGNOSTICS

- Clinical presentation
 - Altered mental status → hyperthermia, rigidity → autonomic dysfunction

TREATMENT**MEDICATIONS**

- Discontinue offending neuroleptic agent
- Dantrolene (skeletal muscle relaxant), bromocriptine (dopamine agonist); both (if severe) to reduce muscle rigidity, hyperthermia

OTHER INTERVENTIONS

- Maintain cardiorespiratory stability
 - Intubation, mechanical ventilation
- Temperature reduction
 - Cooling blankets, ice water gastric lavage, ice packs in axilla; acetaminophen/aspirin
- Correct fluid, electrolyte imbalance
 - ↓ CK damage/accumulation; replete insensible losses from diaphoresis
 - **Benzodiazepines**: ↓ uncontrollable agitations
- Electroconvulsive therapy
 - If not responsive to medical therapy in first week; if severe/lethal catatonia

NEUROLEPTIC MALIGNANT SYNDROME VS. SEROTONIN SYNDROME

	HISTORY	CLINICAL MANIFESTATION	LAB RESULTS	DISTINGUISHING FEATURES
NEUROLEPTIC MALIGNANT SYNDROME	Neuroleptic use	Tetrad: mental status change, fever, rigidity, autonomic instability	↑ CK, leukocytosis, metabolic abnormalities	Severe rigidity, hyperthermia
SEROTONIN SYNDROME	SSRI use	Mental status change, neuromuscular hyperreactivity (tremor, myoclonus), autonomic instability	None consistent with disease; ↑ CPK, leukocytosis, ↓ HCO_3^-	Prodrome of N/V/D; shivering, myoclonus, hyperreflexia, ataxia

PARKINSON'S DISEASE

osms.it/parkinsons-disease

PATHOLOGY & CAUSES

- Degeneration of dopaminergic neurons in substantia nigra → tremor, rigidity, akinesia, postural instability
- Most common neurological disorder; onset after age 50
- Degeneration of neurons in substantia nigra → dopamine depletion from basal ganglia → disruption of connection to thalamus, motor cortex → Parkinsonism
- Exact mechanism unknown; build-up of abnormal proteins into Lewy bodies in neurons; accompanied by death of astrocytes, significant increase in microglia of substantia nigra
- Protein (e.g. alpha-synuclein) accumulation in neuron → abnormal intracellular transit → neuronal damage, death → motor symptoms
 - *Asymptomatic neuronal degeneration:* brainstem (locus coeruleus)
 - *Symptomatic neuronal degeneration:* basal ganglia; dopaminergic substantia nigra pars compacta neurons diseased, die → denervate striatum → dysfunctional basal ganglia → hypo/bradykinetic motor output
 - *Late degeneration:* cerebral cortex; leads to cognitive impairment

CAUSES

- Usually idiopathic
- Mutation of *PINK1*, *parkin*, alpha synuclein genes
- Toxicity in recreational drug MPPP (synthetic opioid); rare

RISK FACTORS

- Family history, previous head injuries, pesticides exposure
- Protective factors
 - Caffeine, nicotine

COMPLICATIONS

- Freezing phenomenon
 - Progressive hypokinesia, bradykinesia → (akinetic) pauses in movement; common when walking; tend to occur at thresholds (e.g. door frames)
- Falls
 - Secondary to postural instability, poor movement amplitude
- Dystonia
 - Abnormal tone across joints → disfiguring, painful posturing; universal flexion of joints → severely kyphotic posturing → poor ability to ambulate, ventilate
- Dementia
 - Common after prolonged, primarily motor disease (in contrast to Lewy body dementia); psychosis, hallucinations (severe)

SIGNS & SYMPTOMS

- Psychiatric
 - Depression, anxiety, mood disturbances; impairment of cognitive function, dementia (advanced stages)
- Sleep disturbances
 - Wild dreams
- Autonomic dysfunction
 - Orthostatic hypotension, constipation, increased sweating
- ↓ olfactory sense
 - Common first symptom; history of ↓ / changed sense of taste, smell prior to motor symptoms
- Micrographia

**MNEMONIC: TRAPS****Parkinson's disease symptoms**

- T**remor (resting tremor)
- R**igidity
- A**kinesia
- P**ostural changes (stooped)
- S**tare (serpentine stare)

**MNEMONIC: SALAD****Common Parkinsonism treatments**

- S**elegiline
- A**nticholinergics: trihexyphenidyl, benhexol, orphenadrine
- L**-Dopa + peripheral decarboxylase inhibitor: carbidopa, benserazide
- A**mantadine
- D**opamine postsynaptic receptor agonists: bromocriptine, lisuride, pergolide

PARKINSON'S DISEASE IMPAIRMENTS

MOTOR IMPAIRMENTS	NON-MOTOR IMPAIRMENTS
- Tremor - Rigid muscles - Difficulty walking - Decreased balance - Freezing of movement - Slowness, decreased amplitude of movement	- Cognitive impairment - Depression, anxiety - Sleep difficulties - Mood disturbances - Decreased motor learning ability

DIAGNOSIS**OTHER DIAGNOSTICS**

- Clinical presentation
 - Resting tremor, rigidity, bradykinesia
 - Dopaminergic medication response
- Postmortem autopsy
 - Loss of pigmented dopaminergic neurons of substantia nigra pars compacta
 - Lewy bodies (intracytoplasmic eosinophilic inclusions), neurites

TREATMENT**MEDICATIONS**

- Symptomatic treatment; see mnemonic

Dopamine replacement

- Precursor to dopamine → ↑ dopamine synthesis → ↑ synaptic dopamine → ↓ motor symptoms
- Commonly formulated with carbidopa (peripheral decarboxylase inhibitor)
 - Carbidopa-mediated inhibition of liver, systemic carboxylation → levodopa cross blood brain barrier (BBB) → ↑ dopamine formation
- Adverse effects
 - **On/off phenomena:** return of symptoms prior to next dose; due to half life of levodopa (approx. 90 minutes)
 - **Dyskinesia, dystonia:** abnormal, repetitive movement (dyskinesia), abnormal sustained muscle contraction (dystonia); head, neck (e.g. tardive dyskinesia of tongue, cervical torticollis); ↑ incidence with ↑ dosing, duration of disease
 - **Neuroleptic malignant syndrome:** when discontinued abruptly/high, multiple doses missed

Dopamine agonists

- ↑ dopaminergic stimulation of postsynaptic receptors → ↓ motor symptoms
- Adverse effects
 - Dyskinesia
 - **Impulse control disorder:** ↑ risk-taking behavior (e.g. pathologic gambling; compulsive sexual behavior, shopping)

Monoamine oxidase B (MAO-B) inhibitors

- ↓ MAO-B-related dopamine metabolism → ↑ synaptic dopamine → ↓ motor symptoms
- Most effective for mild-moderate symptoms

Anticholinergic

- Improves neurochemical imbalance in basal ganglia
- Most useful in young (< 70) individuals with tremor as primary symptom; less useful for rigidity, bradykinesia
- Anticholinergic side effects common

Amantadine

- Antiviral drug
 - Known NMDA receptor agonist; ↓ neurotransmitter imbalance
- Most useful in mild disease

Catechol-O-methyltransferase (COMT) inhibitors

- ↓ dopamine, levodopa metabolism → ↑ synaptic dopamine → ↓ motor symptoms
- Rarely used as monotherapy

SURGERY

- Deep brain stimulation (DBS)
 - Direct neural stimulation of basal ganglia (either subthalamic nucleus or globus pallidus interna) → ↑ motor output of basal ganglia → ↓ motor symptoms
 - Severe/medication nonresponsive disease

OTHER INTERVENTIONS

- Education, support
 - Physical, emotional aspect of degenerative, debilitating disease
- Physical therapy
 - Exercise → ↓ incidence of falls

RESTLESS LEG SYNDROME

osms.it/restless-legs-syndrome

PATHOLOGY & CAUSES

- Uncontrollable urge to move legs, relieved by movement
- Affects legs, feet bilaterally; less commonly affects arms

CAUSES

- Unknown
- CNS
 - ↓ iron, dopamine
- Peripheral nervous system
 - Abnormal A fibers, peripheral nerve microvasculature

TYPES

Primary RLS

- Idiopathic; runs in families; onset < 45 years old; progressive, worsens over time

Secondary RLS

- Associated with underlying medical conditions, medications; onset > 45 years

RISK FACTORS

- Pregnancy, iron deficiency/anemia, smoking, caffeine, Parkinson's disease, family history, renal failure, obesity
- Peripheral neuropathy (due to diabetes, alcoholism, rheumatoid arthritis, etc.)

- Medications
 - Antidepressants, antiemetics, antipsychotics, antihistamines, calcium channel blockers
- More common in individuals who are biologically female

COMPLICATIONS

- Insomnia → daytime drowsiness

SIGNS & SYMPTOMS

- Strong urge to move legs while resting; unpleasant sensations (e.g. tingling, burning, crawling, itching, aching)
- Relief by movement; worsening of symptoms in evening/night → insomnia
- Nighttime leg twitching while asleep

Aggravating factors

- Antihistamines
 - Commonly used for sleep assistance
- Dopamine antagonists
- Psychiatric medications
 - Selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs)

DIAGNOSIS

OTHER DIAGNOSTICS

Clinical Presentation

- Urge to move limbs with/without unpleasant sensations
- Improvement with activity
- Worsening at rest/in evening

TREATMENT

MEDICATIONS

- If other interventions not effective
- Dopamine agonists (e.g. pramipexole, ropinirole)
- Alpha-2-delta calcium channel ligands (e.g. pregabalin, gabapentin)
- Benzodiazepine
 - Individuals with intermittent symptoms
- Iron replacement
 - ↓ symptom severity when low (< 75ng/ml) serum iron levels repleted

OTHER INTERVENTIONS

- Lifestyle changes
 - Avoid aggravating factors/situations, ↓ caffeine intake
- Mental alert activities
 - Distract individual in times of symptoms